Prenatal Maternal Genetic, Permanent Environmental And Paternal Epigenetic Effects In New Zealand Dairy Cattle

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ABSTRACT: 1st lactation milk production data from NZ dairy cows were analyzed using an animal model that included additive genetic, maternal genetic, dam permanent environmental and paternal epigenetic effects. The h^2 estimates varied between 0.267 (protein) and 0.332 (volume), the m^2 between 0.001(fat) and 0.016 (protein) and the pe^2 between 0.000 (fat) and 0.011 (volume). The correlation between the breeding values estimated with and without the maternal genetic and dam permanent environment effects was between 0.97 and 0.98 for all 3 traits. In a separate analysis containing only the additive genetic, maternal genetic and the permanent environmental effects of the sire (paternal epigenetic), the paternal epigenetic heritability was between 0.006 (volume) and 0.014 (protein). The correlation between breeding values estimated with and without the paternal epigenetic effect was between 0.97 and 1.00 for all 3 traits.
Keywords: maternal; permanent environment; epigenetic; Lactation; dairy cattle

Introduction

Dairy calves are typically separated from their mothers soon after birth. Therefore any observed maternal effects can be assumed to have occurred prenatally (Berry et al. (2008), Gudex et al. (2012)). These prenatal effects contain maternal genetic (genetic ability of the dam to provide a suitable environment) and maternal permanent environmental effects (permanent environmental influences on the dam's mothering ability and the maternal non-additive genetic effects of the dam). Cytoplasmic (the effect of DNA that is inherited solely from the dam line within the cytoplasm) and transgenerational epigenetic inheritance (environmentally influenced but heritable changes in gene expression that occur in the absence of changes in the DNA sequence) are examples of maternal non-additive genetic effects that form part of the dam's permanent environmental effect. Cytoplasmic effects have been previously estimated from dairy cattle phenotypic data (e.g. Berry et al. (2008)) and epigenetic effects have not. Using the animal model it is possible to estimate paternal epigenetics by estimating a sire permanent environmental effect in a model that already accounts for additive genetic effects. This works for sires and not dams because there is no possible permanent environmental effect of the sire on the progeny and the non-additive genetic effects of the parent included in the permanent environmental effect cannot include cytoplasmic inheritance (dam only).

The presence of either prenatal maternal effects or transgenerational epigenetics has numerous potential implications for the genetic evaluation of dairy cattle as it may explain some of the missing causality and heritability observed in genomic studies of complex traits and could increase the accuracy of current genetic evaluations by accounting for some of the previously unknown variation (Gonzalez-Recio (2012)). The aim of this study was to estimate prenatal maternal genetic, maternal permanent environmental and paternal epigenetic effects for 1st lactation milk traits in New Zealand dairy cattle.

Materials and Methods

Data. Whole season milk fat (kg), milk protein (kg) and milk volume (L) records were obtained for the 1st lactation (as a 2 year old) of 38929 Holstein Friesian cows born between 1986 and 2011 in LIC's sire proving scheme. The milk production records were yield deviations that were calculated within each contemporary group and corrected to a 270 day lactation. The yield deviations were also corrected for variation in milking frequency and the number and timing of herd tests (for more detail on the yield deviations see Johnson (1996)). Each cow contained a minimum 14/16ths of Holstein Friesian and had high levels of recorded ancestry with 2631 sires, 16706 dams, 309 paternal grand sires and 15402 maternal grand dams in the pedigree file and no unknowns in these categories. There were a total of 3389 contemporary groups, each defined by the cow's birth location and year. All contemporary, sire and dam groups contained multiple progeny to allow the accurate estimation of contemporary group, additive genetic, paternal epigenetic, maternal genetic and permanent environmental effects.

Statistical Analysis. The variance components were estimated for each trait using univariate linear models in ASREML (Gilmour *et al.* (2009)). The model (not all effects fitted in each analysis) was as follows:

$$Y = Xb + Z_1a + Z_2m + Z_3p + Z_4s + e$$

where Y is a vector of the phenotypic performance for each trait within each parity separately; b is a vector of the fixed effect (contemporary group); a is a vector of the individual (additive genetic); m is a vector of dam of the individual (maternal genetic); p is a vector of the permanent environment of the dam (maternal permanent environment); s is a vector of the sire of the individual (fitted independently of any genetic relationships, paternal epigenetic) and e is a vector of residuals. The X and Z matrices are incidence matrices linking the vectors of fixed and random effects,

respectively, to the vector of observations (Y). The model was initially fitted without the sire vector to detect which prenatal maternal/permanent environmental effects were significant and then rerun with the introduction of the sire vector (paternal epigenetic) and the significant prenatal maternal effects.

Results

The maternal genetic variance accounted for less than 2% of the phenotypic variance present in each trait (maternal heritability/m^2, range 0.001 to 0.015) and this proportion was significantly larger than zero ($P<0.05$) for both whole season milk volume and milk protein, but not for milk fat (Table 1). The proportion of the variance explained by the permanent environmental variance was not significant ($P<0.05$) for any of the traits and ranged from 0.000 to 0.011. The additive genetic heritability estimates varied from 0.267 (milk protein) to 0.332 (milk volume). The correlation between breeding values estimated using additive genetic, maternal genetic and permanent environmental effects and those estimated from additive genetic effects only was between 0.97 and 0.98 for all 3 traits.

Table 1: Genetic parameters of whole season milk volume, milk fat and milk protein estimated from a model containing the random effects for additive genetic, maternal genetic and permanent environmental. Standard errors are given for each estimate.

	Milk Volume	Milk Fat	Milk Protein
Phenotypic Variation	208120 litres	328 kg	190 kg
Heritability (h^2)	$0.332\pm0.019^{*}$	$0.264\pm0.017^{*}$	$0.267\pm0.018^{*}$
Maternal Heritability (m^2)	$0.015\pm0.006^{*}$	0.001 ± 0.004^{ns}	$0.016\pm0.007^{*}$
Permanent Environment (pe^2)	0.011 ± 0.009^{ns}	0.000 ± 0.000^{ns}	0.005 ± 0.009^{ns}

* $P < 0.05$; ns = not significantly different from zero.

The results presented in Table 2 are from models that included the sire vector so that the paternal epigenetic heritability could be estimated. The paternal epigenetic heritability was only found to be significantly larger than zero for both milk protein and fat production and not for milk volume. The additive genetic heritability was lower in each trait than what was estimated without the epigenetic effect in the model (Table 1), though the difference was not statistically significant. No consistent differences in maternal heritability were observed between the two models. Although not shown for milk volume and protein, models containing only the additive genetic and paternal epigenetic random effects were also run and the resulting heritability estimates were closer to those estimated using all of the maternal but no epigenetic effects (Table 1) than those estimated using maternal and epigenetic effects (Table 2). The correlation between breeding values estimated using additive genetic, maternal genetic (volume & protein only) and paternal epigenetic and those estimated from additive genetic effects only was between 0.97 and 1.00 for all 3 traits.

Table 2: Genetic parameters of whole season milk volume, milk fat and milk protein estimated from a model containing the random effects for additive genetic, maternal genetic and paternal epigenetics. Standard errors are given for each estimate.

	Milk Volume	Milk Fat	Milk Protein
Phenotypic Variation	207928 litres	328 kg	189 kg
Heritability (h^2)	$0.302\pm0.027^{*}$	$0.260\pm0.016^{*}$	$0.198\pm0.025^{*}$
Maternal Heritability (m^2)	$0.017\pm0.007^{*}$	not in model	$0.014\pm0.007^{*}$
Epigenetic Heritability (e^2)	0.006 ± 0.004^{ns}	$0.007\pm0.003^{*}$	$0.014\pm0.005^{*}$

- $P < 0.05$; ns = not significantly different from zero.
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Discussion

The aim of this study was to estimate prenatal maternal genetic, maternal permanent environmental and paternal epigenetic effects for 1st lactation milk traits in New Zealand dairy cattle. As such, this study represents one of the first attempts at estimating epigenetic effects from phenotypic data in livestock. Transgenerational epigenetics is the occurrence of environmentally influenced but heritable changes in gene expression that occur in the absence of changes in the DNA sequence. This mechanism is thought to allow the organism to have a greater adaptability to short-term environmental shifts without compromising the direction of long-term evolution if the short and long-term requirements are in contrast (Gluckman et al. (2007)). When analyzing epigenetic inheritance, it is important to differentiate between paternal and maternal epigenetic inheritance as each parent can be exposed to different environmental influences. The critical period for exposure to epigenetic causing environmental effects also varies between the sexes, with the production of gametes (by which any epigenetic effects will be transmitted) occurring throughout a male's life but only in the female embryo.

In this study, small (0.7 to 1.4%) but statistically significant amounts of paternal epigenetic inheritance were found for milk fat and protein production. There was also an associated non-statistically significant decrease in (additive genetic) heritability when the epigenetic term was included in the model, though this decrease was not detectable when a simplified model excluding maternal effects was used. This suggests that the model may have had some difficulty in partitioning the total variance amongst its components, though the estimated heritability and maternal heritability were similar to those estimated by Gudex et al. (2012) from a related dataset. The low epigenetic heritabilities observed in this study are consistent with the expectation that bulls owned, raised and maintained in similar environments by a breeding company (in this case, LIC) would be less likely to have variation in epigenetic expression.

Unlike the breeding company owned and maintained bulls, NZ dairy cows are managed under a wide variety of physical environments (e.g. hill versus flat country) and production systems (e.g. once a day versus twice a day milking). Therefore it could be expected that the amount of epigenetic variation arising from the maternal line would be larger. However, the absence in this study of any significant maternal permanent environmental effects (which would include maternal non-additive genetic effects like epigenetic inheritance) suggests that the maternal epigenetics effects would be close to zero for 1st lactation milk traits in this population.

The presence of small but statistically significant maternal heritabilities for milk volume and milk protein confirm the findings of Berry et al. (2008) and Gudex et al. (2012) who found that prenatal maternal genetic effects exist for milk production in dairy cattle. However, given the small size of the prenatal and epigenetic effects (<2% of the phenotypic variation) and the high correlations ($r^2 > 0.97$) between the additive model (no maternal or epigenetic effects) and those estimated using either maternal effects and/or paternal epigenetic effects, there is little value in modifying our current genetic evaluation systems to include either maternal or epigenetic effects for these traits. For further discussion on the potential benefits of incorporating epigenetic effects (if significant) in genetic evaluation, see Gonzalez-Recio (2012).

Dairy cattle (both the animal and its production system) have some unique advantages that make them especially suitable for the investigation of prenatal maternal effects. Not only are the calves hand raised so that no postnatal maternal effects exist but even in commercial herds, dairy cattle have extensive performance and pedigree recording. The life cycle of a dairy cow also makes the existence of prenatal maternal effects more likely than in other livestock species because calves are conceived during the maternal lactation. Therefore the embryo/foetal development has to compete with lactation and other essential biological processes for nutrients and this may affect foetal programming and subsequent adult performance (Berry et al. (2008), Gudex et al. (2012)). The large amount of performance and pedigree recording is counterbalanced partially by the milking performance only being able to be recorded in the females, thus half of the pregnancies do not contribute information unless sexed semen is utilised. This is particularly important when estimating maternal effects as maternal effects require multiple female progeny per dam so that the maternal estimates are formed from more than a single progeny's performance.

Conclusion

This study confirms the unique suitability of dairy cattle for investigating prenatal maternal effects and also represents one of the first attempts at estimating epigenetic effects from phenotypic data in livestock. However, despite their statistical significance, the prenatal maternal and paternal epigenetic effects on 1st lactation performance observed in this study were not of sufficient magnitude to warrant inclusion in commercial genetic evaluations of these traits in New Zealand dairy cattle.

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